# A Draft Immunotoxicity Vocabulary for ToxRefDB

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## ToxRefDB Vocabulary

E	Endpoint super category	Endpoint category	Endpoint subcategory	Endpoint class	Endpoint subclass	Effect type	Effect type	Effect type	Target site a	Target site b
	Developmental		Developmental					Defect A-V	Septum	
	Reproductive	Developmental	Malformation	Cardiovascular	Heart	Developmental	Heart	Septum	Interventricular	[Not Specified]
	Developmental Reproductive	Developmental	DevelopmentalN eurotoxicity	Learning and Memory	Memory	Learning and Memory	Maze	Sector entries	Memory	Radial-arm maze
	Developmental Reproductive	Developmental	PathologyGross	Reproductive Male	Epididymis	Pathology (Gross)	Epididymis	Reduced size	Left	[Not Specified]
H	Reproductive	Developmental	r attiologydioss	iviale	Lpiaidyiiiis	(01033)	Lpialayiiiis	Reduced Size	Leit	[Not specified]
	Developmental		Developmental							
L	Reproductive	Developmental	Malformation	General	Other	Developmental	Thymus	Small	[Not Specified]	[Not Specified]
	Systemic Carcinogenic	Maternal	Pathology Non- Proliferative	Endocrine	Thymus	Pathology (Non- neoplastic)	Thymus	Atrophy	[Not Specified]	[Not Specified]

8834 rows, endpoints for cancer, developmental and reproductive toxicity
Endpoints selected to describe effects, based on toxicity data from testing hundreds of chemicals
In rats and rabbits (http://actor.epa.gov/toxrefdb/faces/BasicInfo.jsp)
Search by endpoint (study type, species, effect type) to return list of chemicals associated with effect
(http://actor.epa.gov/toxrefdb/faces/SearchByEndpoint.jsp)

### **Immunotoxicity Classification**

- Immunosuppression (immunostimulation)
- Allergic hypersensitivity
- Autoimmunity
- Endpoints are relevant for adult and developmental exposure effects

## **Immunotox Endpoint Interpretation**

	Indicator	Assessment	Function	Interpretation		
	Lymphoid organ data	Weights, cellularity, viability, architecture	Maturation, differentiation	Suggestive		
<b>y</b>	Cell surface markers	Flow cytometry	Relative distribution by function/type	Suggestive/confirmatory		
Complexity	Cytokine production	mRNA, protein, activity	Regulation, modulation of cell proliferation, maturation, function	Suggestive/confirmatory		
Specificity, (	Innate immunity	Activation, phagocytosis killing, mediator production	Resistance to infection	Intracellular & extracellular infection, viral infections, tumors		
— Sp	Antibody synthesis	TDAR: "PFC" or ELISA response	Resistance to infection Toxin neutralization	Extracellular infection, viral infections, tetanus		
	Cell mediated immunity	Delayed hypersensitivity Cytotoxicity Cytokine production	Resistance to infection, neoplasia "Help" for Ig response	Intracellular infection, viral infections, tumors		

## Draft immunotox vocabulary content

- Borrowed entries from exiting ToxRefDB that may indicate immune system effects
- Added new categories, subcategories endpoint classes and subclasses, effect types and targets that may be generated in immunotoxicity studies

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		T	T	T		T	T	T	
Endpoint super category	Endpoint category	Endpoint subcategory	Endpoint class	Endpoint subclass	Effect type	Effect type	Effect type	Target site a	Target site b
Immunotoxicity	Adult Immunotoxicity	Immuno- suppression	Host resistance	Bacterial challenge	Immuno- suppression	Humoral Immunity	Infection resistance	B Lymphocyte	IgM
Immunotoxicity	Adult immunotoxicity	Immuno- suppression	Immune Function	Humoral Immunity	Immuno- suppression	Humoral Immunity	Infection resistance	B Lymphocyte	IgM
Immunotoxicity	Adult immunotoxicity	Immuno- suppression	Immune Function	Cellular Immunity	Immuno- suppression	Cellular Immunity	Infection/tumor resistance	T helper 1 Lymphocyte	Delayed Hypersensitivity
Immunotoxicity	Adult immunotoxicity	Immuno- suppression	Immune Function	Innate immunity	Immuno- suppression	Innate immunity	Infection/tumor resistance	Natural Killer Cell	Target cell lysis
Immunotoxicity	Adult immunotoxicity	Immuno- suppression	Immune Observation	Lymphocyte Proliferation	Immuno- suppression	Cellular Immunity	Mitogen Response	T Lymphoocyte	Cellular Immunity
Immunotoxicity	Adult immunotoxicity	Immuno- suppression	Immune Observation	Hematology	Immuno- suppression	Hematology	Complete Blood Count	Leukocyte	Cell Number
Immunotoxicity	Adult Immunotoxicity	Immuno- suppression	In-Life Observations	Clinical Signs	In-Life Observations	Clinical Signs	Skin Lesion (infection)	н	IgM
Immunotoxicity	Adult immunotoxicity	Immuno- suppression	ImmuneFunction	Humoral Immunity	Immunostimulati on	Humoral Immunity	Stimulation	Dendritic Cell	Infection/Autoim munity
Immunotoxicity	Adult Immunotoxicity	Allegic Hypersensitivity	ImmuneFunction	Humoral Immunity	Antibody synthesis	Humoral Immunity	Anaphylaxis	Lung	IgE
Immunotoxicity	Adult Immunotoxicity	Allegic Hypersensitivity	ImmuneFunction	Local Lymph Node Assay	ImmuneFunction	Contact hypersensitivity	Contact hypersensitivity	Lymph Node	Proliferation
Immunotoxicity	Adult Immunotoxicity	Allegic Hypersensitivity	ImmuneFunction	Mouse Ear Swelling Test	Immune Function	Contact hypersensitivity	Contact hypersensitivity	Ear	Swelling
Immunotoxicity	Adult immunotoxicity	Autoimmunity	Immune Observation	Humoral Immunity	Antibody synthesis	Self Antigens	Autoimmunity	Autoantibody	Anti-dsDNA
Immunotoxicity	Adult immunotoxicity	Autoimmunity	Immune Observation	Humoral Immunity	Autoimmunity	Kidney	Autoimmunity	kidney	Proteinuria
Immunotoxicity	Developmental immunotoxicity	Same as adult	Same as adult	Same as adult	Same as adult	Same as adult	Same as adult	Same as adult	Same as adult

#### **Next Steps and Caveats**

- Incorporate into ToxRefDB
- Test ability to capture immunotox data in published studies
- Minimal outside input on entries
- Is the structure adaptable to other vocabularies?